Labeling Guidance
Revised August 1993

SULFAMETHOXAZOLE AND TRIMETHOPRIM TABLETS USP
SULFAMETHOXAZOLE AND TRIMETHOPRIM ORAL SUSPENSION USP

DESCRIPTION

Sulfamethoxazole and trimethoprim tablets/oral suspension is a synthetic antibacterial combination product.

Sulfamethoxazole is N^1-(5-methyl-3-isoxazolyl)sulfanilamide. It is a white to off-white, practically odorless, crystalline powder with a molecular weight of 253.28 and the following structural formula:

$C_{10}H_{11}N_3O_3S$

Trimethoprim is 2,4-diamino-5-(3,4,5-trimethoxybenzyl)pyrimidine. It occurs as white to cream-colored, odorless crystals, or crystalline powder with a molecular weight of 290.32 and the following structural formula:

$C_{14}H_{18}N_4O_3$

[Include type of dosage form, strength, and route of administration, e.g., Each tablet, for oral administration contains...]

[*NOTE*: *In accordance with good pharmaceutical practice, all dosage forms should be labeled to cite all inactive ingredients (refer to USP General Chapter <1091> for guidance). We believe this is an important public health measure. Please respond by noting the inactive ingredients present in this product.*]

CLINICAL PHARMACOLOGY

Sulfamethoxazole and trimethoprim is rapidly absorbed following oral administration. Both sulfamethoxazole and trimethoprim exist in the blood as unbound, protein-bound and metabolized forms; sulfamethoxazole also exists as the conjugated form. The metabolism of

sulfamethoxazole occurs predominately by N_4-acetylation, although the glucuronide conjugate has been identified. The principal metabolites of trimethoprim are the 1- and 3-oxides and the 3'- and 4'- hydroxy derivatives. The free forms of sulfamethoxazole and trimethoprim are considered to be the therapeutically active forms. Approximately 70% of sulfamethoxazole and 44% of trimethoprim are bound to plasma proteins. The presence of 10 mg percent sulfamethoxazole in plasma decreases the protein binding of trimethoprim by an insignificant degree; trimethoprim does not influence the protein binding of sulfamethoxazole.

Peak blood levels for the individual components occur 1 to 4 hours after oral administration. The mean serum half-lives of sulfamethoxazole and trimethoprim are 10 and 8 to 10 hours, respectively. However, patients with severely impaired renal function exhibit an increase in the half-lives of both components, requiring dosage regimen adjustment (see **DOSAGE AND ADMINISTRATION** section). Detectable amounts of sulfamethoxazole and trimethoprim are present in the blood 24 hours after drug administration. During administration of 800 mg sulfamethoxazole and 160 mg trimethoprim *b.i.d.*, the mean steady state plasma concentration of trimethoprim was 1.72 µg/mL. The steady state minimal plasma levels of free and total sulfamethoxazole were 57.4 µg/mL and 68.0 µg/mL, respectively. These steady state levels were achieved after three days of drug administration. [1]

Excretion of sulfamethoxazole and trimethoprim is primarily by the kidneys through both glomerular filtration and tubular secretion. Urine concentrations of both sulfamethoxazole and trimethoprim are considerably higher than are the concentrations in the blood. The average percentage of the dose recovered in urine from 0 to 72 hours after a single oral dose is 84.5% for total sulfonamide and 66.8% for free trimethoprim. Thirty percent of the total sulfonamide is excreted as free sulfamethoxazole, with the remaining as N_4-acetylated metabolite. [2] When administered together, neither sulfamethoxazole nor trimethoprim affects the urinary excretion pattern of the other.

Both sulfamethoxazole and trimethoprim distribute to sputum, vaginal fluid, and middle ear fluid; trimethoprim also distributes to bronchial secretion and both pass the placental barrier and are excreted in human milk.

Microbiology
Sulfamethoxazole inhibits bacterial synthesis of dihydrofolic acid by competing with *para*-aminobenzoic acid (PABA). Trimethoprim blocks the production of tetrahydrofolic acid from dihydrofolic acid by binding to and reversibly inhibiting the required enzyme, dihydrofolate reductase. Thus, this combination blocks two consecutive steps in the biosynthesis of nucleic acids and proteins essential to many bacteria.

In vitro studies have shown that bacterial resistance develops more slowly with this combination than with either sulfamethoxazole or trimethoprim alone.

In vitro serial dilution tests have shown that the spectrum of antibacterial activity of sulfamethoxazole and trimethoprim includes the common urinary tract pathogens with the exception of *Pseudomonas aeruginosa*. The following organisms are usually susceptible: *Escherichia coli*, *Klebsiella* species, *Enterobacter* species, *Morganella morganii*, *Proteus mirabilis* and indole-positive *Proteus* species including *Proteus vulgaris*.

The usual spectrum of antimicrobial activity of sulfamethoxazole and trimethoprim includes bacterial pathogens isolated from middle ear exudate and from bronchial secretions (*Haemophilus influenzae*, including ampicillin-resistant strains, and *Streptococcus pneumoniae*), and enterotoxigenic strains of *Escherichia coli* (ETEC) causing bacterial gastroenteritis. *Shigella flexneri* and *Shigella sonnei* are also usually susceptible.

REPRESENTATIVE MINIMUM INHIBITORY CONCENTRATION VALUES FOR SULFAMETHOXAZOLE AND TRIMETHOPRIM SUSCEPTIBLE ORGANISMS (MIC-µg/mL)

Bacteria	TMP Alone	SMX Alone	TMP/SMX (1:19) TMP	SMX
Escherichia coli	0.05-1.5	1.0-245	0.05-0.5	0.95-9.5
Escherichia coli (enterotoxigenic strains)	0.015-0.15	0.285->950	0.005-0.15	0.095-2.85
Proteus species (indole positive)	0.5-5.0	7.35-300	0.05-1.5	0.95-28.5
Morganella morganii	0.5-5.0	7.35-300	0.05-1.5	0.95-28.5
Proteus mirabilis	0.5-1.5	7.35-30	0.05-0.15	0.95-2.85
Klebsiella species	0.15-5.0	2.45-245	0.05-1.5	0.95-28.5
Enterobacter species	0.15-5.0	2.45-245	0.05-1.5	0.95-28.5
Haemophilus influenzae	0.15-1.5	2.85-95	0.015-0.15	0.285-2.85
Streptococcus pneumoniae	0.15-1.5	7.35-24.5	0.05-0.15	0.95-2.85
Shigella flexneri†	<0.01-0.04	<0.16->320	<0.002-0.03	0.04-0.625
Shigella sonnei†	0.02-0.08	0.625->320	0.004-0.06	0.08-1.25

TMP=Trimethoprim : SMX=Sulfamethoxazole

†Rudoy RC, Nelson JD, Haltalin KC. *Antimicrobial Agents And Chemotherapy* 5:439-43, 1974.

Susceptibility Testing

The recommended quantitative disc susceptibility method may be used for estimating the susceptibility of bacteria to sulfamethoxazole and trimethoprim. [3,4] With this procedure, a report from the laboratory of "Susceptible to sulfamethoxazole and trimethoprim" indicates that the infection is likely to respond to therapy with this product. If the infection is confined to the urine, a report of "Intermediate susceptibility to sulfamethoxazole and trimethoprim" also indicates that the infection is likely to respond. A report of "Resistant to sulfamethoxazole and trimethoprim" indicates that the infection is unlikely to respond to therapy with this product.

INDICATIONS AND USAGE

Urinary Tract Infections
For the treatment of urinary tract infections due to susceptible strains of the following organisms: *Escherichia coli*, *Klebsiella* species, *Enterobacter* species, *Morganella morganii*, *Proteus mirabilis*, and *Proteus vulgaris*. It is recommended that initial episodes of uncomplicated urinary tract infections be treated with a single effective antibacterial agent rather than the combination.

Acute Otitis Media
For the treatment of acute otitis media in children due to susceptible strains of *Streptococcus pneumoniae* or *Haemophilus influenzae* when in the judgment of the physician this combination offers some advantage over the use of other antimicrobial agents. To date, there are limited data on the safety of repeated use of sulfamethoxazole and trimethoprim in children under two years of age. This product is not indicated for prophylactic or prolonged administration in otitis media at any age.

Acute Exacerbations Of Chronic Bronchitis In Adults
For the treatment of acute exacerbations of chronic bronchitis due to susceptible strains of *Streptococcus pneumoniae* or *Haemophilus influenzae* when in the judgment of the physician, this combination offers some advantage over the use of a single antimicrobial agent.

Travelers' Diarrhea In Adults
For the treatment of travelers' diarrhea due to susceptible strains of enterotoxigenic *E. coli*.

Shigellosis
For the treatment of enteritis caused by susceptible strains of *Shigella flexneri* and *Shigella sonnei* when antibacterial therapy is indicated.

***Peumocystis Carinii* Pneumonia**
For the treatment of documented *Pneumocystis carinii* pneumonia.

CONTRAINDICATIONS

Hypersensitivity to trimethoprim or sulfonamides. Patients with documented megaloblastic anemia due to folate deficiency. Pregnancy at term and during the nursing period, because sulfonamides pass the placenta and are excreted in the milk and may cause kernicterus. Infants less than two months of age.

WARNINGS

FATALITIES ASSOCIATED WITH THE ADMINISTRATION OF SULFONAMIDES, ALTHOUGH RARE, HAVE OCCURRED DUE TO SEVERE REACTIONS, INCLUDING STEVENS-JOHNSON SYNDROME, TOXIC EPIDERMAL NECROLYSIS, FULMINANT HEPATIC NECROSIS, AGRANULOCYTOSIS, APLASTIC ANEMIA, OTHER BLOOD DYSCRASIAS AND HYPERSENSITIVITY OF THE RESPIRATORY TRACT.

SULFAMETHOXAZOLE AND TRIMETHOPRIM SHOULD BE DISCONTINUED AT THE FIRST APPEARANCE OF SKIN RASH OR ANY SIGN OF ADVERSE REACTION. Clinical signs, such as rash, sore throat, fever, arthralgia, cough, shortness of breath, pallor, purpura or jaundice may be early indications of serious reactions. Cough, shortness of breath, and/or pulmonary infiltrates may be indicators of pulmonary hypersensitivity to sulfonamides. In rare instances a skin rash may be followed by more severe reactions, such as Stevens-Johnson syndrome, toxic epidermal necrolysis, hepatic necrosis or serious blood disorder. Complete blood counts should be done frequently in patients receiving sulfonamides.

SULFAMETHOXAZOLE AND TRIMETHOPRIM SHOULD NOT BE USED IN THE TREATMENT OF STREPTOCOCCAL PHARYNGITIS. Clinical studies have documented that patients with group A beta-hemolytic streptococcal tonsillopharyngitis have a greater incidence of bacteriologic failure when treated with this combination than do those patients treated with penicillin, as evidenced by failure to eradicate this organism from the tonsillopharyngeal area.

PRECAUTIONS

General

Sulfamethoxazole and trimethoprim should be given with caution to patients with impaired renal or hepatic function, to those with possible folate deficiency (e.g., the elderly, chronic alcoholics, patients receiving anticonvulsant therapy, patients with malabsorption syndrome, and patients in malnutrition states) and to those with severe allergy or bronchial asthma. In glucose-6-phosphate dehydrogenase-deficient individuals, hemolysis may occur. This reaction is frequently dose-related. (See **CLINICAL PHARMACOLOGY** and **DOSAGE AND ADMINISTRATION**.)

Use In The Elderly
There may be an increased risk of severe adverse reactions in elderly patients, particularly when complicating conditions exist, e.g., impaired kidney and/or liver function, or concomitant use of other drugs. Severe skin reactions, or generalized bone marrow suppression (see **WARNINGS** and **ADVERSE REACTIONS** sections) or a specific decrease in platelets (with or without purpura) are the most frequently reported severe adverse reactions in elderly patients. In those concurrently receiving certain diuretics, primarily thiazides, an increased incidence of thrombocytopenia with purpura has been reported. Appropriate dosage adjustments should be made for patients with impaired kidney function (see **DOSAGE AND ADMINISTRATION** section).

Use In The Treatment Of *Pneumocystis Carinii* Pneumonia In Patients With Acquired Immunodeficiency Syndrome (AIDS)
The incidence of side effects, particularly rash, fever, leukopenia, and elevated aminotransferase (transaminase) values with sulfamethoxazole and trimethoprim therapy in AIDS patients who are being treated for *Pneumocystis carinii* pneumonia has been reported to be greatly increased compared with the incidence normally associated with the use of sulfamethoxazole and trimethoprim in non-AIDS patients.

Information For Patients
Patients should be instructed to maintain an adequate fluid intake in order to prevent crystalluria and stone formation.

Laboratory Tests
Complete blood counts should be done frequently in patients receiving sulfamethoxazole and trimethoprim; if a significant reduction in the count of any formed blood element is noted, this drug product should be discontinued. Urinalysis with careful microscopic examination and renal function tests should be performed during therapy, particularly for those patients with impaired renal function.

Drug Interactions
In elderly patients concurrently receiving certain diuretics, primarily thiazides, an increased incidence of thrombocytopenia with purpura has been reported.

It has been reported that sulfamethoxazole and trimethoprim may prolong the prothrombin time in patients who are receiving the anticoagulant warfarin. This interaction should be kept in mind when sulfamethoxazole and trimethoprim is given to patients already on anticoagulant therapy, and the coagulation time should be reassessed. Sulfamethoxazole and trimethoprim may inhibit the hepatic metabolism of phenytoin. Given at a common clinical dosage, it increased the phenytoin half-life by 39% and decreased the phenytoin metabolic clearance rate by 27%. When administering these drugs concurrently,

one should be alert for possible excessive phenytoin effect.

Sulfonamides can also displace methotrexate from plasma protein binding sites, thus increasing free methotrexate concentrations.

Drug/Laboratory Test Interactions
This combination product, specifically the trimethoprim component, can interfere with a serum methotrexate assay as determined by the competitive binding protein technique (CBPA) when a bacterial dihydrofolate reductase is used as the binding protein. No interference occurs, however, if methotrexate is measured by a radioimmunoassay (RIA). The presence of sulfamethoxazole and trimethoprim may also interfere with the Jaffé alkaline picrate reaction assay for creatinine resulting in over-estimations of about 10% in the range of normal values.

Carcinogenesis, Mutagenesis, Impairment of Fertility

Carcinogenesis: Long-term studies in animals to evaluate carcinogenic potential have not been conducted with sulfamethoxazole and trimethoprim.

Mutagenesis: Bacterial mutagenic studies have not been performed with sulfamethoxazole and trimethoprim in combination. Trimethoprim was demonstrated to be non-mutagenic in the Ames assay. In studies at two laboratories no chromosomal damage was detected in cultured Chinese hamster ovary cells at concentrations approximately 500 times human plasma levels; at concentrations approximately 1000 times human plasma levels in these same cells a low level of chromosomal damage was induced at one of the laboratories. No chromosomal abnormalities were observed in cultured human leukocytes at concentrations of trimethoprim up to 20 times human steady state plasma levels. No chromosomal effects were detected in peripheral lymphocytes of human subjects receiving 320 mg of trimethoprim in combination with up to 1600 mg of sulfamethoxazole per day for as long as 112 weeks.

Impairment of Fertility: No adverse effects on fertility or general reproductive performance were observed in rats given oral dosages as high as 350 mg/kg/day sulfamethoxazole and 70 mg/kg/day trimethoprim.

Pregnancy
Teratogenic Effects: Pregnancy Category C. In rats, oral doses of 533 mg/kg sulfamethoxazole or 200 mg/kg trimethoprim produced teratological effects manifested mainly as cleft palates. The highest dose which did not cause cleft palates in rats was 512 mg/kg sulfamethoxazole or 192 mg/kg trimethoprim when administered separately. In two studies in rats, no teratogenicity was observed

when 512 mg/kg of sulfamethoxazole was used in combination with 128 mg/kg of trimethoprim. In one study, however, cleft palates were observed in one litter out of 9 when 355 mg/kg of sulfamethoxazole was used in combination with 88 mg/kg of trimethoprim.

In some rabbit studies, an overall increase in fetal loss (dead and resorbed and malformed conceptuses) was associated with doses of trimethoprim 6 times the human therapeutic dose.

While there are no large, well-controlled studies on the use of sulfamethoxazole and trimethoprim in pregnant women, Brumfitt and Pursell[5], in a retrospective study, reported the outcome of 186 pregnancies during which the mother received either placebo or sulfamethoxazole and trimethoprim. The incidence of congenital abnormalities was 4.5% (3 of 66) in those who received placebo and 3.3% (4 of 120) in those receiving sulfamethoxazole and trimethoprim. There were no abnormalities in the 10 children whose mothers received the drug during the first trimester. In a separate survey, Brumfitt and Pursell also found no congenital abnormalities in 35 children whose mothers had received oral sulfamethoxazole and trimethoprim at the time of conception or shortly thereafter.

Because sulfamethoxazole and trimethoprim may interfere with folic acid metabolism, this product should be used during pregnancy only if the potential benefit justifies the potential risk to the fetus.

Nonteratogenic Effects: See **CONTRAINDICATIONS** section.

Nursing Mothers
See **CONTRAINDICATIONS** section.

Pediatric Use
Sulfamethoxazole and trimethoprim is not recommended for infants younger than two months of age (see **INDICATIONS AND USAGE** and **CONTRAINDICATIONS** sections).

ADVERSE REACTIONS

The most common adverse effects are gastrointestinal disturbances (nausea, vomiting, anorexia) and allergic skin reactions (such as rash and urticaria). **FATALITIES ASSOCIATED WITH THE ADMINISTRATION OF SULFONAMIDES, ALTHOUGH RARE, HAVE OCCURRED DUE TO SEVERE REACTIONS, INCLUDING STEVENS-JOHNSON SYNDROME, TOXIC EPIDERMAL NECROLYSIS, FULMINANT HEPATIC NECROSIS, AGRANULOCYTOSIS, APLASTIC ANEMIA, OTHER BLOOD DYSCRASIAS AND HYPERSENSITIVITY OF THE RESPIRATORY TRACT (SEE WARNINGS SECTION)**.

Hematologic
Agranulocytosis, aplastic anemia, thrombocytopenia, leukopenia,

neutropenia, hemolytic anemia, megaloblastic anemia, hypoprothrombinemia, methemoglobinemia, eosinophilia.

Allergic
Stevens-Johnson syndrome, toxic epidermal necrolysis, anaphylaxis, allergic myocarditis, erythema multiforme, exfoliative dermatitis, angioedema, drug fever, chills, Henoch-Schoenlein purpura, serum sickness-like syndrome, generalized allergic reactions, generalized skin eruptions, photosensitivity, conjunctival and scleral injection, pruritus, urticaria and rash. In addition, periarteritis nodosa and systemic lupus erythematosus have been reported.

Gastrointestinal
Hepatitis including cholestatic jaundice and hepatic necrosis, elevation of serum transaminase and bilirubin, pseudomembranous enterocolitis, pancreatitis, stomatitis, glossitis, nausea, emesis, abdominal pain, diarrhea, anorexia.

Genitourinary
Renal failure, interstitial nephritis, BUN and serum creatinine elevation, toxic nephrosis with oliguria and anuria, and crystalluria.

Neurologic
Aseptic meningitis, convulsions, peripheral neuritis, ataxia, vertigo, tinnitus, headache.

Psychiatric
Hallucinations, depression, apathy, nervousness.

Endocrine
The sulfonamides bear certain chemical similarities to some goitrogens, diuretics (acetazolamide and the thiazides) and oral hypoglycemic agents. Cross-sensitivity may exist with these agents. Diuresis and hypoglycemia have occurred rarely in patients receiving sulfonamides.

Musculoskeletal
Arthralgia and myalgia.

Respiratory System
Pulmonary infiltrates, cough, shortness of breath.

Miscellaneous
Weakness, fatigue, insomnia.

OVERDOSAGE

Acute

The amount of a single dose of sulfamethoxazole and trimethoprim that is either associated with symptoms of overdosage or is likely to be life-threatening has not been reported. Signs and symptoms of overdosage reported with sulfonamides include anorexia, colic, nausea, vomiting, dizziness, headache, drowsiness and unconsciousness. Pyrexia, hematuria and crystalluria may be noted. Blood dyscrasias and jaundice are potential late manifestations of overdosage. Signs of acute overdosage with trimethoprim include nausea, vomiting, dizziness, headache, mental depression, confusion and bone marrow depression. General principles of treatment include the institution of gastric lavage or emesis; forcing oral fluids; and the administration of intravenous fluids if urine output is low and renal function is normal. Acidification of the urine will increase renal elimination of trimethoprim. The patient should be monitored with blood counts and appropriate blood chemistries, including electrolytes. If a significant blood dyscrasia or jaundice occurs, specific therapy should be instituted for these complications. Peritoneal dialysis is not effective and hemodialysis is only moderately effective in eliminating sulfamethoxazole and trimethoprim.

Chronic
Use of sulfamethoxazole and trimethoprim at high doses and/or for extended periods of time may cause bone marrow depression manifested as thrombocytopenia, leukopenia and/or megaloblastic anemia. If signs of bone marrow depression occur, the patient should be given leucovorin; 5 to 15 mg leucovorin daily has been recommended by some investigators.

DOSAGE AND ADMINISTRATION

Contraindicated in infants less than two months of age.

URINARY TRACT INFECTIONS AND SHIGELLOSIS IN ADULTS AND CHILDREN AND ACUTE OTITIS MEDIA IN CHILDREN:

Adults
The usual adult dosage in the treatment of urinary tract infections is one double strength tablet, two single strength tablets or four teaspoonfuls (20 mL) of the suspension every 12 hours for 10 to 14 days. An identical daily dosage is used for 5 days in the treatment of shigellosis.

Children
The recommended dose for children with urinary tract infections or acute otitis media is 40 mg/kg sulfamethoxazole and 8 mg/kg trimethoprim per 24 hours, given in two divided doses every 12 hours for 10 days. An identical daily dosage is used for 5 days in the treatment of shigellosis. The following table is a guideline for the

attainment of this dosage:

Children: Two Months Of Age Or Older

WEIGHT		DOSE--EVERY 12 HOURS	
lb	kg	Teaspoonfuls	Tablets
22	10	1 (5 mL)	
44	20	2 (10 mL)	1
66	30	3 (15 mL)	1 ½
88	40	4 (20 mL)	2 (or 1 DS Tablet)

For Patients With Impaired Renal Function
When renal function is impaired, a reduced dosage should be employed using the following table:

Creatinine Clearance (mL/min)	Recommended Dosage Regimen
Above 30	Use Standard Regimen
15 to 30	½ the Usual Regimen
Below 15	Use Not Recommended

ACUTE EXACERBATIONS OF CHRONIC BRONCHITIS IN ADULTS
The usual adult dosage in the treatment of acute exacerbations of chronic bronchitis is one double strength tablet, two single strength tablets or four teaspoonfuls (20 mL) of the suspension every 12 hours for 14 days.

TRAVELERS' DIARRHEA IN ADULTS
For the treatment of travelers' diarrhea, the usual adult dosage is one double strength tablet, two single strength tablets or four teaspoonfuls (20 mL) of the suspension every 12 hours for 5 days.

PNEUMOCYSTIS CARINII PNEUMONIA
The recommended dosage for patients with documented *Pneumocystis Carinii* pneumonia is 100 mg/kg sulfamethoxazole and 20 mg/kg trimethoprim per 24 hours given in equally divided doses every 6 hours for 14 days. The following table is a guideline for the attainment of this dosage in children:

WEIGHT		DOSE--EVERY 6 HOURS	
lb	kg	Teaspoonfuls	Tablets
18	8	1 (5 mL)	
35	16	2 (10 mL)	1
53	24	3 (15 mL)	1 ½
70	32	4 (20 mL)	2 (or 1 DS Tablet)

HOW SUPPLIED

-Established Name and Strength
-Packaging
-Shape, color, coating, scoring, debossing, or imprinting
-NDC
-Special handling and storage conditions
-Caution: Federal law...

REFERENCES

1. Kremers P, Duvivier J, Heusghem C. Pharmacokinetic studies of co-trimoxazole in man after single and repeated doses. *J Clin Pharmacol*. 1974; 14:112-117.
2. Kaplan SA, Weinfeld RE, Abruzzo CW, McFaden K, Jack ML, Weissman L. Pharmacokinetic profile of trimethoprim-sulfamethoxazole in man. *J Infect Dis*. November 1973; 128(suppl):S547-S555.
3. Antibiotic susceptibility discs: certification procedure. *Fed Reg*. 37:20527-20529, 1972.
4. Bauer AW, Kirby WMM, Sherris JC, Turck M. Antibiotic susceptibility testing by standardized single disk method. *Am J Clin Pathol*. 1966; 45:493-496.
5. Brumfitt W, Pursell R. Trimethoprim-sulfamethoxazole in the treatment of bacteriuria in women. *J Infect Dis*. November 1973; 128(suppl):S657-S663.

Date of latest revision

Manufactured by statement